

Efficacy of protected renal artery primary stenting in the solitary functioning kidney

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Background: Significant renal artery stenosis (RAS) in a solitary functioning kidney (SFK) represents one of the most acceptable indications for renal revascularization. Percutaneous transluminal renal artery stenting (PTRAS) is increasingly being used as a first line treatment for renal revascularization, associated with renal function improvement or stabilization in the majority of the patients with solitary kidneys, but also with deterioration in up to 38% of the cases. Atheroembolism during PTRAS has been postulated as a potential cause for this acute renal function worsening. The aim of this study was to report on the feasibility, safety, and early outcomes of PTRAS in a series of patients with SFK using distal embolic protection (DEP).

Methods: All PTRAS procedures in SFKs performed under DEP between June 2002 and September 2007 were reviewed. Renal function, blood pressure, and the number of anti-hypertensive medications were assessed pre- and post-intervention. Renal function improvement and deterioration were defined as a 20% increase and decrease in serum creatinine, respectively, compared with preoperative values. Primary and primary assisted patency rates were also calculated. Statistical differences between values before and after intervention were determined by the Student t test and statistical significance was taken at $P < .05$.

Results: Protected PTRAS was performed in 14 patients with a SFK (9 men, 6 women, mean age 65.6 ± 6.8 years). All patients were hypertensive and had varying degrees of azotemia. Mean pre-intervention stenosis degree was $86.8\% \pm 7.8\%$. Immediate technical success was obtained in 100% of the patients. Renal function was cured (7.1%), improved (50%), or stabilized (42.9%) in all 14 (100%) patients after the procedure and no deterioration was noticed in any patient at 6-month follow-up. Pre- and postintervention serum creatinine levels were 3.01 ± 1.15 mg/dL and 2.16 ± 0.68 mg/dL, respectively, ($P = .02$). Hypertension was improved in 6 (42.9%) patients and stabilized in the remaining 8 (57.1%). Primary patency was 100% and 90% at 1 and 3 years, respectively, while primary assisted patency remained 100% for the whole follow-up period (mean, 31.8 ± 19.4 months).

Conclusion: These findings suggest that in patients with a SFK, protected PTRAS represents a safe and effective treatment for halting the progression of renal dysfunction to renal loss and warrants further investigation. (*J Vasc Surg* 2008;48:1414-22.)

Renovascular disease is considered to be responsible for approximately 12% of end-stage renal disease (ESRD) cases.¹ The progressive nature of renal artery stenosis (RAS) and its adverse effects in the cardiovascular system, renal function, and survival have been well established.^{2,3} The severity of RAS pattern directly affects survival; 2-year dialysis-free survival has been reported to be 97.3% for patients with unilateral RAS, 82.4% for patients with bilateral RAS but only 44.7% in patients with renovascular disease in a solitary functioning kidney.² Over the last decades, RAS has been recognized as a potentially correctable cause of hypertension and renal insufficiency⁴ and revascularization with endovascular techniques is currently advocated by many clinicians in an attempt to preserve renal function especially in individuals with solitary functioning kidneys (SFKs).

To date, only a small number of studies have evaluated the efficacy of percutaneous transluminal renal artery stent-

ing (PTRAS) in patients with SFKs.⁵⁻¹⁰ Although PTRAS was shown to improve or stabilize renal function in the majority of the patients, it was also associated with renal function deterioration in 13-38% of the cases. Based on the hypothesis that this phenomenon may be partly or totally due to distal atheroembolization during the procedure, we investigated the use of distal embolic protection (DEP) devices in patients undergoing primary stenting of the renal artery for solitary kidney salvage. To our knowledge, this is the first series in the literature reporting the outcomes of protected PTRAS in the SFK.

METHODS

Patients. The medical records of all patients with RAS in a SFK that were treated with PTRAS under distal embolic protection during the period from June 2002 to September 2007 were retrospectively analyzed for this study. Materials reviewed included records from the outpatient clinic, noninvasive vascular laboratory, and hospital and endovascular operating suites that provided information about patients' demographics, indications for intervention, procedural details and complications, postoperative course, and renal artery patency during follow-up. Primary or referring physicians were also contacted for additional information and data.

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Competition of interest: none.

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Preoperative imaging evaluation included color duplex ultrasonography scan and digital subtraction angiography (DSA). All patients were admitted to our department the day before the procedure for overnight intravenous hydration.

Indications for treatment included a hemodynamically significant RAS ($\geq 60\%$ as measured at DSA) in a SFK with length ≥ 80 mm. All patients provided informed consent before the procedure.

Procedure. All interventions were performed under local anesthesia in the endovascular suite. A retrograde femoral approach was utilized in 13 cases, while in 1 patient with acute aorto-renal angle the procedure was performed through right brachial artery catheterization. A bolus of 5000 IU of intravenous heparin was administered routinely once access was obtained. Selective cannulation of the renal artery was achieved with a 7F angled guiding catheter (Renal Double Curve). The lesion to be treated was not crossed with the guide catheter. Subsequently, the distal protection filter device (EX/EZ Filterwire, Boston Scientific Corporation, Natick, Mass; $n = 10$, RX Accunet, Abbott Vascular, Abbott Park, Ill; $n = 4$) was advanced and deployed at the distal main renal artery. Complete filter apposition to the vessel wall was checked with fluoroscopy in at least two oblique views looking for contrast floating around the filter. Afterwards, balloon expandable stents were positioned and deployed primarily without predilation, with a slight protrusion of 1-2 mm into the aortic lumen, while also covering the whole length of the lesion to be treated. Predilation was avoided in order to minimize debris dislodgement before covering the lesion with the stent. Sizing of the stents was based on the diameter of the distal healthy main renal artery. Six stents (42.9%) were inflated up to 5 mm, while the remaining 8 (57.1%) up to 6 mm. Regarding stent length, we used the shorter stent that was adequate to cover the whole stenosed segment.

After stent deployment and arteriographic confirmation of satisfactory stent placement, the filter was recaptured. The particles collected in the filter were sent for pathologic analysis. Hemostasis was achieved with local pressure alone at the puncture site. The iodinated contrast (Ultravist-300, Schering, Germany, concentration: 300 mgI/mL) was diluted by half during the procedure; its amount was closely monitored and never exceeded 50 mL.

After the procedure, double antiplatelet treatment with aspirin (100 mg/day) and clopidogrel (75 mg/day) was administered for 1 month, and then monotherapy with aspirin (100 mg/day) was continued long term.

Patients remained in the hospital for 48 hours to monitor their serum creatinine and adjust their antihypertensive drugs.

Follow-up imaging studies with renal artery color duplex scanning were scheduled at 3 and 6 months postintervention and then biannually. DSA was performed only when significant restenosis was suspected due to positive clinical and ultrasound scan findings and reintervention was considered. Serum creatinine levels were measured 1 day before and after the procedure and at 1, 3, and 6 months,

with biannual measurements thereafter by the primary-referring physicians of the patients.

Definitions, outcome measures, and statistical analysis. Lesions were considered ostial if they involved the first 5 mm of the main renal artery.¹¹ The arterial stenosis degree was calculated at duplex ultrasonography scan (renal artery peak systolic velocity [PSV] >1.8 m/second and presence of poststenotic turbulence for determining a hemodynamically significant stenosis)¹² and was confirmed at angiogram by comparing the narrowest lumen of the renal artery with the nearest normal distal lumen unaffected by post-stenotic dilatation.

Immediate technical success was defined as safely crossing and stenting the stenosis with no significant procedural complications, a residual stenosis $<30\%$ of the reference diameter as measured on angiogram and no flow-limiting intimal dissection.¹³ Inability to place the filter successfully at the correct position and/or to achieve complete apposition with the vessel wall to protect the renal parenchyma throughout the procedure was considered to be device failure.

Blood pressure (BP) changes were assessed on the basis of the criteria established by the cooperative study on renovascular hypertension.¹⁴ A diastolic pressure of 90 mm Hg or less without anti-hypertensive medication was considered cured. A decrease in diastolic pressure of 15% or more without any change in the number of anti-hypertensive medications was considered an improvement. Failure was considered an increase of 15% or more in the diastolic pressure after stenting. The rest of the cases were classified as stable.

Moderate renal insufficiency was defined as baseline serum creatinine ≥ 1.5 and <2.0 mg/dL, while creatinine values ≥ 2.0 mg/dL were categorized as severe renal insufficiency.^{11,15}

Renal function improvement was defined as a decrease of 20% or more in the serum creatinine level postintervention (1 and 6 months) compared to the preoperative baseline level. An increase of 20% or more from baseline level was classified as deterioration in renal function and creatinine values within 20% of baseline were considered to be unchanged.^{5,8} Renal function cure was defined as serum creatinine ≤ 1.4 mg/dL after the procedure.

Restenosis was defined as a decrease in renal artery diameter $\geq 50\%$ detected by duplex ultrasonography scan (renal artery PSV >2.2 m/second) and confirmed at DSA during follow-up. Primary patency was defined as patent stents (stenosis $<50\%$) detected at duplex ultrasound scan during follow-up without any further intervention, while primary assisted patency was defined as patent stents (stenosis $<50\%$) after successful additional percutaneous procedures.⁷

Statistical analysis was done with SPSS 10.0 software (SPSS Inc, Chicago, Ill). Continuous data are presented as mean \pm standard deviation (SD) and categorical data as percentages. Statistical differences between groups were determined by the Student *t* test. Statistical significance was

Table I. Patient demographics (n = 14)

Gender (M:F)	9:5 (64.3:35.7%)
Age (years)	65.6 ± 6.8 (range, 48-72)
Risk factors (n = 14)	
Smoking history	10 (71.4%)
Coronary artery disease	9 (64.3%)
Diabetes mellitus	5 (35.7%)
Peripheral arterial disease	8 (57.2%)
Blood pressure (mm Hg)*	
Systolic	171.8 ± 10.7 (range, 162-205)
Diastolic	92.1 ± 4.3 (range, 91-110)
Number of antihypertensive drugs*	2.8 ± 0.6 (range, 2-4)
Serum creatinine level (pre-procedure)*	3.01 ± 1.15 mg/dL (range, 1.6-6.1 mg/dL)

*Expressed as mean ± standard deviation.

taken at $P < .05$. The persistence of patency during follow-up was reported by Kaplan-Meier analysis.

RESULTS

From June 2002 to September 2007, 14 patients (9 men; mean age 65.6 ± 6.8 years) who were diagnosed with RAS to a SFK were treated with percutaneous primary stenting under filter protection.

Patients' demographics are shown in Table I. All patients suffered from hypertension and were on antihypertensive medications (2-4 drugs). Seven (50%) patients had an occluded contralateral renal artery, 5 (35.7%) had had a previous nephrectomy due to trauma or malignancy and 2 (14.3%) had a congenital solitary kidney.

All had varying degrees of azotemia (mean serum creatinine 3.01 ± 1.15 mg/dL); 3 (21.4%) patients had moderate renal insufficiency, 10 (71.4%) had severe renal dysfunction and 1 (7.1%) presented with acute solitary renal artery occlusion (serum creatinine: 6.1 mg/dL). None of the patients was on hemodialysis before revascularization.

The stenosis was located at the ostium of the solitary renal artery in all 14 (100%) cases. Mean degree of stenosis was $86.8\% \pm 7.8\%$ (range, 70%-100%). Mean lesion length was 14.2 ± 2.9 mm (range, 9-19 mm). The normal diameter of the artery was estimated at 5 mm in 6 cases and 6 mm in 8 cases. Eleven (78.6%) patients had diffuse atherosclerosis of the abdominal aorta. One patient also had a 5.4 cm abdominal aortic aneurysm (AAA) that was treated with a two-stage procedure consisted of initial PTRAS followed by endovascular aneurysm repair (EVAR) 2 weeks later. A second patient suffered from a 6.4 cm type III thoracoabdominal aortic aneurysm (TAAA) and a 4.2 cm infrarenal AAA; the TAAA was treated with endovascular techniques 1 month after renal stenting, while the AAA is still being under surveillance.

All 14 lesions were treated with primary stenting. Fourteen balloon-expandable stents of different types according to operator choice (Corinthian, n = 2, Cordis Endovascular, Warren, NJ; Herculink, n = 7, Abbott Vascular, Abbott Park, Ill; Express, n = 5; Boston Scientific Corporation, Natick, Mass) were advanced and placed at the appropriate position in main renal artery under filter protection. All 14

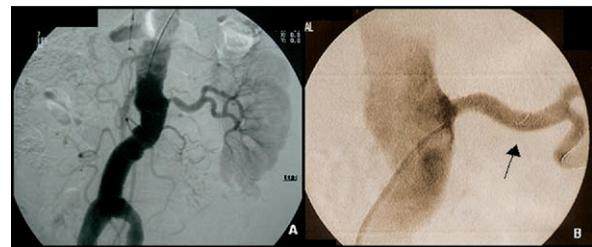


Fig 1. A, Preoperative DSA demonstrating a significant left renal artery ostial stenosis in a solitary functioning kidney. B, Angiogram after stent placement showing successful revascularization without residual stenosis. Note the contrast floating around the filter due to incomplete apposition to the vessel wall (arrow).

patients required only one stent for complete covering of their lesion. Immediate technical success was obtained for all 14 arteries (100%) with good stent deployment, no significant residual stenosis, and complete lesion coverage.

All lesions were easily crossed with the protection filters while there were no difficulties in removing the protection filters. In 12 out of 14 cases, complete apposition of the filter to the vessel wall was achieved, while there were two device failures, where there was contrast floating around the filter due to increased main renal artery diameter (Fig 1). The mean time in situ for filters was 4.6 ± 1.12 minutes. One patient developed an arterial spasm at the site of the protection filter, which responded well to local vasodilation therapy. No dissection of the vessel artery due to a protection filter was observed in these 14 cases.

Macroscopic visible debris collected in the filter was found in nine cases (64.3%); while microscopic evaluation detected particles in 11 of 14 filters (78.6%). The remainder of the baskets were either empty or contained insufficient material to survive processing. Qualitative analysis with light microscopy revealed that the particles consisted of atheromatous plaques, cholesterol crystals, necrotic cores, fibrin, thrombi, platelets, and macrophage foam cells.

Follow-up. The mean follow-up period was 31.8 ± 19.4 months (range, 6-67 months). In all cases, follow-up was beyond the period for development of clinical manifestations of atheroembolism.¹⁶ Two patients died from myo-

Table II. Statistical significance between baseline and post-interventional values

Variable	Baseline	Post-interventional	P
Systolic blood pressure (mm Hg)*	171.8 ± 10.7 (162-205)	150.4 ± 25.9 (120-196)	.017
Diastolic blood pressure (mm Hg)*	92.1 ± 4.3 (91-110)	80.9 ± 14.6 (68-107)	.008
Number of anti-hypertensive medications*	2.8 ± 0.6 (2-4)	1.8 ± 1.1 (1-4)	.002
Serum creatinine level (mg/dL)*	3.01 ± 1.15 (1.6-6.1)	2.16 ± 0.68 (1.2-3.9)	.02

*Expressed as mean ± standard deviation (range).

Table III. Clinical outcome after stenting (n = 14)

	Cured	Improved	Stabilized	Deteriorated
Hypertension	0	6 (42.9%)	8 (57.1%)	0
Creatinine	1 (7.2%)	7 (50%)	6 (42.8%)	0
Antihypertensive drug number	0	9 (64.3%)	5 (35.7%)	0

cardial infarction, one at 1-year follow-up and one at 18 months after the procedure. One patient was lost to follow-up after 12 months.

Renal function was cured (7.1%), improved (50%), or stabilized (42.9%) in all 14 (100%) patients after the procedure and no deterioration was noticed in any patient until the 6-month follow-up. Additionally, there was a statistically significant reduction in the mean serum creatinine level from 3.01 ± 1.15 mg/dL preprocedurally to 2.16 ± 0.68 mg/dL 1-month post intervention that was sustained (2.16 ± 0.59 mg/dL) at 6-month follow-up. Exclusion from the analysis of the patient with the outlier serum creatinine value of 6.1 mg/dL that is very likely to represent an acute on chronic renal failure situation and not a steady state chronic creatinine level, revealed a less marked, but still statistically significant decrease in the mean serum creatinine level (2.78 ± 0.76 mg/dL preprocedurally to 2.24 ± 0.65 mg/dL 1-month postintervention and 2.2 ± 0.6 mg/dL 6 months after the procedure, $P < .05$). No patient required dialysis during the long-term follow-up (mean 31.8 ± 19.4 months).

Regarding the effects of the procedure on hypertension, there was a statistically significant reduction in both systolic ($P = .017$) and diastolic BP ($P = .008$) and in the number of anti-hypertensive drugs ($P = .002$) after PTRAS. In addition, hypertension was improved in 6 (42.9%) patients and remained unchanged in 8 (57.1%) after the procedure (Tables II and III).

No 30-day mortality was observed in this series. One (7%) patient developed a minor access-site hematoma that was treated nonoperatively. In-stent restenosis was detected in 2 patients in this series. The first one was detected at 15 months after the procedure and was successfully treated with angioplasty. At 30 months, a new restenosis was found at the distal edge of the previously placed stent and a 6 mm × 22 mm balloon-expandable covered stent was placed (Advanta V12, Atrium Medical, Hudson, NH) without residual stenosis. Distal embolic protection was not used in any of these two procedures due to technical

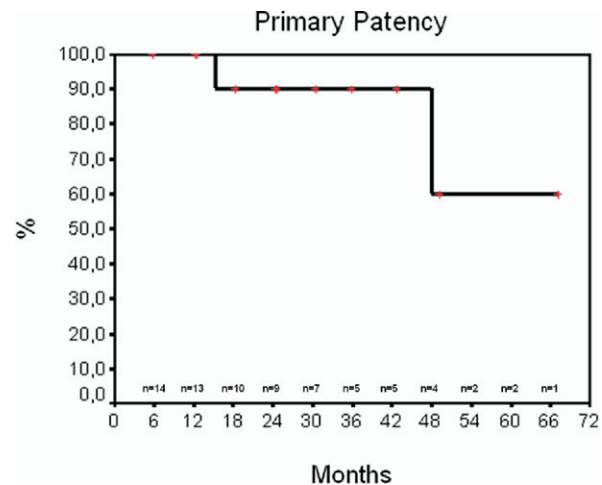


Fig 2. Kaplan-Meier analysis of primary patency after protected renal artery stenting in the solitary functioning kidney.

difficulties owing to the protrusion of the proximal edge of the renal stent in the aortic lumen. The second patient suffered an in-stent restenosis at 48 months and was treated successfully with stenting under filter protection. Until the most recent available follow-up, both these patients were doing well without any signs of recurrent stenosis. Kaplan-Meier analysis of primary patency is shown in Fig 2. Primary patency was 100% and 90% at 1 and 3 years, respectively, while primary assisted patency remained 100% for the whole follow-up period (mean, 31.8 ± 19.4 months).

DISCUSSION

Renal artery stenosis in the SFK represents the most severe pattern of renovascular disease; patients with a significant RAS to a SFK are at a markedly increased risk of renal loss. In this patient population, the probability of total renal artery occlusion is high, and if this occurs, the outcome is abrupt loss of functioning renal mass, with resulting renal failure.^{4,17} Additionally, ischemic nephropathy or flash pulmonary edema almost always occurs in the presence of bilateral RAS or disease in a SFK.⁴ Moreover, 2-year dialysis-free survival has been reported to be only 44.7% in case of RAS in a SFK, in contrast to 97.3% for patients with unilateral disease.² Thus, revascularization of the SFK is advocated in an effort to halt the progression of renal dysfunction and most importantly to prevent kidney loss. Indeed, RAS in a SFK is among factors that may predict a

favorable response to revascularization.¹⁸ The need for interventional treatment of a RAS in a SFK owing to the dismal prognosis of these patients is well reflected in the latest American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines; RAS to a single functioning kidney in patients with progressive chronic kidney disease represents the indication with the highest level of evidence (level B) for percutaneous revascularization as an attempt to preserve renal function.¹⁹

Renal artery revascularization may also be useful in hypertension control. Current evidence supports that patients with severe atherosclerotic RAS and accelerated, resistant, or malignant hypertension may expect to receive some clinical benefit after renal revascularization.¹⁹ Especially for patients with a SFK, RAS treatment may also allow for long-term administration of otherwise contraindicated angiotensin antagonist medications with additional benefits in cardiovascular risk reduction.¹⁹

Endovascular therapy including percutaneous transluminal renal angioplasty (PTRA) and stenting has emerged as an advantageous treatment strategy for renovascular disease during the last 2 decades. Stent placement in the renal artery ostium significantly improves primary and secondary patency rates compared with PTRA alone as previously outlined by Blum et al¹¹ and other authors.^{11,20-23} The superiority of stenting has been also confirmed in a recent randomized trial,²⁴ where stent implantation in ostial atherosclerotic RAS was associated with a higher primary success rate (88% vs 57%) and a lower restenosis rate (14% vs 48%), in comparison with PTRA.

However, despite the high technical success rate, long-term patency and low complication rates, PTRAS often fails to improve or stabilize renal function. Indeed, renal function deterioration may occur in a significant proportion of patients after renal percutaneous revascularization,^{25,26} limiting, thus, the benefits of the procedure. Several explanations have been proposed for this phenomenon including contrast media-induced nephrotoxicity, unsuspected irreversibility of pre-existing renal parenchyma damage, progression of atherosclerosis, reperfusion injury, and most importantly, atheroembolism during angioplasty and stenting.²⁷⁻²⁹

Atheroemboli to the kidney, beyond mechanical occlusion of smaller vessels distal to the stenosis is also known to cause local vascular inflammation resulting in substantial renal parenchyma damage. It has been suggested that atherogenic lipoproteins contained in released atheroemboli along with circulating cytokines may induce endothelial- and epithelial-cell dysfunction and vascular damage distal to the stenosis and infiltrate the mesangium and blood vessels.³⁰ This promotes growth factor secretions that result in glomerular and vascular remodeling and proliferation of extracellular matrix.²⁷ Prognosis of atheroembolic renal disease (AERD) is poor; up to 40-50% of the patients will require dialysis, while complete recovery of renal function is expected to only one-fifth to one-third of the patients.^{31,32} Unfortunately, several factors such as the uncertain incidence, insidious and nonspecific clinical manifestations,

and difficulty for definite diagnosis contribute to underestimation or misdiagnosis of AERD after renal artery interventions in clinical practice.

Nevertheless, there is increasing evidence that PTRAS produce atheroembolic debris that can strongly affect renal function. Ex vivo manipulation of the atheromatous renal artery ostium has been shown to release large numbers of embolic particles during angioplasty and stenting.²⁸ Additionally, a recent in vivo study demonstrated that on average 2000 atheroembolic particles are liberated during renal artery angioplasty and stenting, while the increasing particle count was found to be significantly and independently associated with the extent of short-term renal function impairment post intervention.³³ Moreover, Al-Hamali et al³⁴ has demonstrated that Doppler scan embolic signals can be recorded over the femoral arteries for 2 hours after renal angioplasty, implying that there is significant debris release during renal angioplasty. Finally, Kimura et al³⁵ injected different numbers of acryl bead microspheres to mimic atheroembolic disease in rats; interestingly, the outcomes in terms of renal dysfunction were dependent on the initial dose of microspheres and only the largest dose resulted in renal function decline indicating that there may be a dose-effect relationship in AERD.

According to the aforementioned considerations, it was speculated that reduction or even elimination of atheroembolic debris generated during the procedure could potentially improve the results of endoluminal renal artery interventions. Beyond the "no touch" technique proposed by Feldman et al,³⁶ few investigators published their experience with renal angioplasty and stenting under DEP^{29,37-39} particularly in patients with unilateral disease. These studies demonstrated the feasibility and safety of the procedure and revealed the beneficial role of DEP, documenting zero or very low rates of renal function impairment (0-3%) after PTRAS.

Based on these limited but promising results derived particularly from patients with unilateral RAS, we were prompted to investigate the use of DEP in individuals with a SFK, who probably represent the most vulnerable patient population for developing renal failure after an atheroembolic event during PTRAS. In this series, all 14 ostial atherosclerotic lesions were primarily stented under DEP with favorable results. Renal function was cured or improved in 57.2% and stabilized in the remaining 42.8%. These results are in agreement with the aforementioned series using DEP in patients unilateral disease.^{38,40}

To date, only a small number of studies⁵⁻¹⁰ documenting percutaneous revascularization in the SFK exist in the literature, all without the use of DEP (Table IV). In these series, renal function was improved in 21-62% and stabilized in 19-55%, but it was also acutely deteriorated in 13-38% of the patients after percutaneous revascularization. Compared with these previously published series, our results represent a marked improvement in terms of short-term renal function response rates after PTRAS, since there was no renal function worsening in any of our patients. This is of great significance especially in light of already pub-

Table IV. Results of renal artery stenting in the solitary functioning kidney

<i>Author</i>	<i>No. of cases</i>	<i>Technical success (%)</i>	<i>Complications (%)</i>	<i>Effect on renal function</i>	<i>Effect on hypertension</i>	<i>Mean follow-up (range)¹</i>	<i>Primary patency (%)</i>
Shannon ¹⁰	21	100	28.6	43% Improvement 29% Stabilization 29% Deterioration		15	100 ²
Bush ⁵	27	93	22	46% Improvement 28% Stabilization 25% Deterioration		20.7 ± 17 (0.3-60.2)	
Cioni ⁷	16	100	0	62% Improvement 19% Stabilization 19% Deterioration	88% Improvement 13% Stabilization 0% Deterioration	21 (6-36)	75 ³
Chatziioannou ⁶	26	100	8	35% Improvement 27% Stabilization 38% Deterioration		3	
Sahin ⁸	15	100	26.8	60% Improvement 27% Stabilization 13% Deterioration	6.7% Cure 26.6% Improvement 66.7% Stabilization 0% Deterioration	(12-60)	69.2 ³
Tan ⁹	75	100	25	21% Improvement 55% Stabilization 21% Deterioration	22% Improvement 70% Stabilization 7% Deterioration	12	
Present study	14	100	7.2	7.1% Cure 50% Improvement 42.9% Stabilization 0% Deterioration	42.9% Improvement 57.1% Stabilization 0% Deterioration	31.8 ± 19.4 (6-67)	100 ⁴ 90 ⁵

¹Follow up duration is expressed in months.

²Primary patency at 9 months.

³Primary patency at 24 months.

⁴Primary patency at 12 months.

⁵Primary patency at 36 months.

lished data indicating that short-term renal function response following PTRAS is a robust predictor of subsequent morbidity and mortality.^{38,41,42} We hypothesize that this is probably due to the reduction/elimination of atheroembolization during the procedure owing mainly to the use of DEP devices. To our knowledge, no other series exists in the literature focusing on the efficacy of DEP during PTRAS in the SFK.

In this series, all RAS were directly stented successfully without predilation, which may have also contributed in the zero rate of renal function deterioration succeeded in our patients. Indeed, covering the lesion with a stent before angioplasty may reduce the possibility of distal embolization, since the potentially embolic material is trapped between the stent and the arterial wall. Prospective randomized studies are necessary in order to definitely clarify this issue; however, since such evidence is not currently available, the decision regarding predilation of a RAS is based mainly on arbitrary data and physicians' personal opinion.

As already noticed, additional mechanisms other than atheroembolism may also contribute to renal function deterioration after PTRAS including progression of atherosclerosis, reperfusion injury, and contrast-induced nephrotoxicity.²⁷ However, our findings indicate that atheroembolism may probably be the most significant factor affecting renal function after PTRAS, since elimi-

nation of distal emboli with DEP utilization resulted in prevention of renal function worsening in all patients.

Despite the good overall results in this patient cohort with the use of DEP, it should be noticed that embolic protection filters still have limitations that can potentially jeopardize the success of percutaneous renal artery interventions. Filter placement and deployment represent an additional step to the procedure and carry a small, but existent risk of complications such as arterial dissection, spasm, or intimal damage. Additionally, particles smaller than 100 µm, which is the average filter pore size of the majority of commercially available filters, are not captured and can occlude the afferent arteriole and/or glomerulus.²⁸ Moreover, in several cases, renal artery shows early branching with a short main renal artery; this can make it difficult or impossible to anchor the filter distally enough in order to secure access and have adequate stability to advance the stent and at the same time protect the whole kidney rather than only a portion supplied by one renal artery division. In such cases, the use of eccentric filters with a beveled ring (eg, EZ/EX Filterwire, Boston Scientific Corporation) may be preferential (Fig 3). In addition, the "short renal artery phenomenon" may also compromise the ability to get the stiffer-working portion of the wire well seeded into the main renal artery across the target lesion. Of note, during the time frame of the study, 2 patients with SFK were judged unfit for filter placement due to early

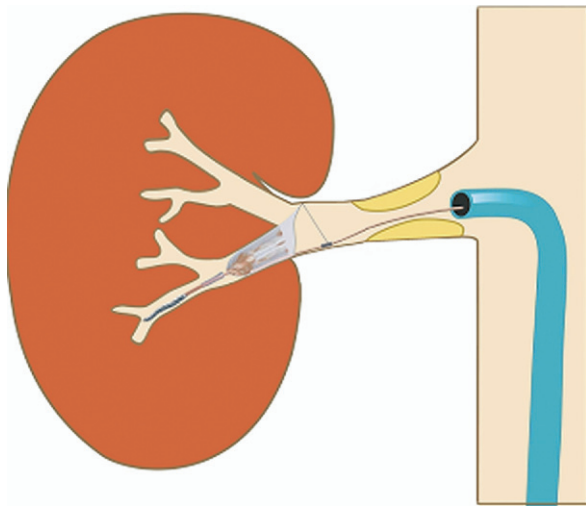


Fig 3. Drawing shows the use of an eccentric filter with a beveled ring in order to provide complete renal protection in cases of short main renal artery; the tip of the filter is anchored distally in one renal artery branch, while the proximal beveled part of the basket remains in the main renal artery protecting both renal artery divisions.

bifurcation of the main renal artery and were stented without DEP, thus, being excluded from the present series. Finally, some filters are designed for vessel diameters up to 5.5 mm, which in some cases may be slightly smaller than the main renal artery that ranges from 5.5 to 7 mm, thus resulting in incomplete apposition of the filter to the vessel wall and debris floating around the filter loop. The latter did indeed occur in 2 of our patients without, however, any apparent clinical sign of distal embolization. In any case, however, even “partial protection” is probably preferable to “no protection”.³⁵

Currently, all embolic protection devices have been designed and approved for use in coronary saphenous vein grafts and carotid artery stenting, while their use in the renal artery has been extended “off label”. Appropriate refinements in filter engineering with filters designed specifically for renal artery anatomy are necessary before filter embolic protection technology can be used to its full advantage in renal percutaneous revascularization procedures. More specifically, in comparison with the currently available filter devices, renal artery filters should ideally have: (1) Lower profile and better flexibility, pushability, and maneuverability in order to deal with the perpendicular access needed due to the acute aortorenal angle. (2) Increased guidewire strength so as to minimize the need for very distal anchoring and facilitate stent advancement over the aortorenal junction. (3) Reduced landing zone requirements so that it can be used even in cases of early renal artery bifurcation. (4) Shorter length of the floppy portion of the wire. (5) Availability of larger ring diameters up to 7 mm in order to provide complete vessel wall apposition in all cases. (6) Different mesh structure to capture particles

smaller than 100 μm , which can occlude the afferent arteriole and/or glomerulus.²⁸

Blood pressure improvement was observed in 42.9% of our patients. Review of other series reveals a great variation in BP response to percutaneous revascularization of the SFK ranging from 22-88%.^{7,9} Several factors may be responsible for this variance, including different follow-up periods, perhaps too short in some studies to allow for BP improvement detection, coexisting severe essential hypertension in some patient cohorts, lack of down-regulation of the renin-angiotensin system due to suboptimal PTRAS results, etc. Obviously, additional studies are required in order to clearly illustrate the role of renal percutaneous revascularization in BP control in patients with a SFK. In any case, it should be noticed that although the extent of the benefit after PTRAS in terms of hypertension treatment cannot be accurately predicted, the probability of BP deterioration is extremely low (5 out of 194 patients including our series), making PTRAS a safe procedure. Additionally, as it has been shown by other series and confirmed by our study, PTRAS apart from BP decrease, results also in a significant decline in the number of antihypertensive medications used, a fact with important social and financial implications.

Despite the promising results, this study has several limitations. The small cohort of patients may have limited the expected number of adverse events and potentially increased the chance of counterfeit positive results. Moreover, it may also have limited the existence of unfavorable anatomy not allowing the use of DEP, such as in patients with early main renal artery bifurcation. Although such difficulties did not occur in our study, it is undoubtful that they will be observed with widespread use of protection filters in renal interventions. Most importantly, the results of this study were not compared with an identical randomized control group of patients undergoing renal artery stenting without DEP.

However, our findings demonstrate the safety and feasibility of DEP in the SFK and probably imply that filter protection devices should be routinely used in this “delicate” patient population where an atheroembolic event during catheter-based manipulations could potentially lead even to renal failure and hemodialysis, since there is no healthy contralateral kidney to compensate for reduced function in the ischemic kidney. Although to date there are no established selection criteria for DEP use in renal interventions, we believe that RAS in a SFK may represent one of the most appropriate clinical scenarios that routine use of DEP could be recommended. Certainly, further prospective randomized clinical trials are necessary before generalized utilization of filters in percutaneous revascularization of SFKs can be justified. It is of note that the impact of DEP in renal percutaneous interventions is mirrored in the design of the Cardiovascular Outcomes with Renal Atherosclerotic Lesions (CORAL) study, which is a multicenter, randomized trial aiming to compare best medical therapy vs best medical therapy plus PTRAS; in the stent group filter

embolic protection will be used whenever feasible, as determined by the interventionalists.^{4,3}

CONCLUSION

This study evaluated renal artery primary stenting under DEP in the SFK. Our results demonstrate that this technique is feasible, safe, and effective associated with renal function improvement or stabilization in all patients along with a marked decline in BP in a significant portion of cases. In contrast with previously published series reporting PTRAS in the SFK, in our study no short-term renal function deterioration was noticed in any of the patients after PTRAS. This may well be attributed to the prevention of distal atheroembolism during stenting owing mainly to the use of DEP and implies a beneficial role of protection devices in the “borderline group” of patients with RAS in a SFK.

AUTHOR CONTRIBUTIONS

Conception and design: CK, AK
Analysis and interpretation: CK, AK, AA, CT, AG, EB
Data collection: CK, AK, AA, AG, EB
Writing the article: CK, AK, AA, CT, AG
Critical revision of the article: CK, AK, AA, CT, AG, EB
Final approval of the article: CK, AK, AA, CT, AG, EB
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